REMARKS

Applicants thank Examiners Crouch and Woitach for the interview conducted June 25, 2002, and present in this communication the amendments discussed in that interview.

At the onset, Applicants point out that the claims have now been amended to require the expression of a "soluble" chemokine. This additional limitation further distinguishes the invention from the prior art. Applicants' specification, for example, at page 11 (lines 8-11) supports such amendment, where it is disclosed that successful high-level synthesis of secreted chemokines was achieved using a Sendai virus expression system. Applicants' further teach, in Example 3, the purification of chemokines SDF-1α and SDF-1β from culture supernatant, and Example 4 teaches that both chemokines were "functionally authentic." Clearly, in view of the cited references inability to produce soluble, biologically active chemokines, both the suggestion and the incentive to produce chemokines using a Sendai virus expression system are absent. The cited references do not indicate that Sendai virus is a useful host for expressing soluble, biologically active chemokine: There is nothing in any of the references to suggest that the claimed invention would be successful, and, in fact, the references teach away from the claimed invention. Furthermore, the references do not convey to those of ordinary skill a reasonable expectation of success in producing soluble, biologically active chemokine using a Sendai virus vector.

With respect to the phrase "a substantial amount," this phrase has been removed from the claims, obviating any rejection under 35 U.S.C. § 112, second paragraph. Similarly, Applicants note that the term "promoters" is not used in the claims and therefore does not raise any issue under §112, second paragraph.

Finally, on the issue of workability of the therapeutic method claims, Applicants direct the Examiner's attention to MPEP 2107.03 (III) and case law cited therein, which states:

> If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays ... almost invariably will be sufficient to establish the therapeutic or pharmacological utility for a ... process.

As noted in previous correspondence, Applicants, in their specification, have plainly demonstrated that a recombinant chemokine, encoded on a Sendai virus vector, had anti-HIV activity *in vitro*. As direct evidence of this point, Applicants direct the Examiner's attention to the specification, for example, at pages 10-14, where it was demonstrated that not only were substantial amounts of the chemokine, SDF-1α, produced in a chicken embryo fibroblast host cell using the disclosed recombinant Sendai virus expression vector system (see, Example 2, pages 10-11), but also that this chemokine had anti-HIV activity (see, Example 4, pages 11-14). Here Applicants demonstrated that recombinant SDF-1α suppressed the replication of **three different T cell line tropic HIV-1 strains**: NL43, SF33, and TK11, in the MT4 cell line, and one syncytium inducing primary isolate (page, 13, lines 21-23). Moreover, both SDF-1α and

SDF-1β suppressed HIV-1 strain NL43. This evidence clearly demonstrates the workability of the claimed therapeutic methods.

CONCLUSION

In view of the above, Applicants submit that the claims are now in condition for allowance, and such action is requested. A marked-up version of the claims indicating the amendments made to those claims is enclosed. A clean version of all pending claims is also enclosed.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Version with Markings to Show Changes Made

Claims 1-3, 6-7, 10-12, and 14-15 are amended as follows.

1. (Twice Amended) A recombinant Sendai virus vector expressing a [substantial amount of] soluble and biologically active chemokine.

2. (Amended) The recombinant Sendai virus vector of claim 1, wherein said chemokine is soluble and biologically active CXC-chemokine.

3. (Amended) The recombinant Sendai virus vector of claim 2, wherein said CXC-chemokine is soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β.

6. (Twice Amended) A method of producing a [substantial amount of] soluble and biologically active chemokine which comprises inserting at least one chemokine gene into a Sendai virus vector, allowing the vector to produce said chemokine, and recovering said chemokine.

7. (Amended) The method of claim 6, wherein said chemokine is soluble and biologically active CXC-chemokine.

10. (Three Times Amended) A method of treating human immunodeficiency virus infection, which comprises collecting target cells from human subjects, infecting the cells with a recombinant Sendai virus vector expressing a [substantial amount of] soluble and biologically active CXC-chemokine, and returning the infected cells to the human subjects.

11. (Twice Amended) A pharmaceutical composition comprising a recombinant Sendai virus vector expressing a [substantial amount of] soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β and a pharmaceutically acceptable carrier, wherein said vector is disseminative.

12. (Twice Amended) A pharmaceutical composition comprising a recombinant Sendai virus vector expressing a [substantial amount of] soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β and a pharmaceutically acceptable carrier, wherein said vector is infectious and replicates autonomously, but is not disseminative.

14. (Twice Amended) A host cell transfected with a recombinant Sendai virus vector exp . sing a [substantial amount of] soluble and biologically active chemokine.

15. (Three Times Amended) A method of inhibiting proliferation of HIV-infected cells *in vitro* which comprises, incubating the host cell of claim 14 *in vitro* under conditions that allow for secretion of a [substantial amount of] soluble and biologically active chemokine; and contacting said chemokine with cells that are infected with HIV, thereby inhibiting proliferation of HIV-infected cells *in vitro*.

The following new claims 16-23 are added:

16. (New) The method of claim 7, wherein said CXC-chemokine is soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β.

17. (New) The method of claim 7, wherein the step of recovering comprises the step of removing virions by centrifugation.

18. (New) The method of claim 16, wherein the step of recovering comprises the step of removing virions by centrifugation.

19. (New) The method of claim 10, wherein said CXC-chemokine is soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β.

20. (New) The host of claim 14, wherein said chemokine is soluble and biologically active CXC-chemokine.

21. (New) The host of claim 20, wherein said CXC-chemokine is soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β.

22. (New) A method of inhibiting proliferation of HIV-infected cells *in vitro* which comprises, incubating the host cell of claim 20 *in vitro* under conditions that allow for secretion of soluble and biologically active CXC-chemokine; and contacting said CXC-chemokine with cells that are infected with HIV, thereby inhibiting proliferation of HIV-infected cells *in vitro*.

23. (New) A method of inhibiting proliferation of HIV-infected cells *in vitro* which comprises, incubating the host cell of claim 21 *in vitro* under conditions that allow for secretion of soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β and contacting said stromal cell-derived factor α or stromal cell-derived β with the cells that are infected with HIV, thereby inhibiting proliferation of HIV-infected cells *in vitro*.

Clean Version of Pending Claims

1. (Twice Amended) A recombinant Sendai virus vector expressing a soluble and biologically active chemokine.

2. (Amended) The recombinant Sendai virus vector of claim 1, wherein said chemokine is soluble and biologically active CXC-chemokine.

3. (Amended) The recombinant Sendai virus vector of claim 2, wherein said CXC-chemokine is soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β.

4. The recombinant Sendai virus vector of claim 3, wherein said vector is disseminative.

5. The recombinant Sendai virus vector of claim 3, wherein said vector is infectious and replicates autonomously, but is not disseminative.

6. (Twice Amended) A method of producing a soluble and biologically active chemokine which comprises inserting at least one chemokine gene into a Sendai virus vector, allowing the vector to produce said chemokine, and recovering said chemokine.

7. (Amended) The method of claim 6, wherein said chemokine is soluble and biologically active CXC-chemokine.

8. The method of claim 6, wherein the step of recovering comprises the step of removing virions by centrifugation.

10. (Three Times Amended) A method of treating human immunodeficiency virus infection, which comprises collecting target cells from human subjects, infecting the cells with a recombinant Sendai virus vector expressing a soluble and biologically active CXC-chemokine, and returning the infected cells to the human subjects.

11. (Twice Amended) A pharmaceutical composition comprising a recombinant Sendai virus vector expressing a soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β and a pharmaceutically acceptable carrier, wherein said vector is disseminative.

12. (Twice Amended) A pharmaceutical composition comprising a recombinant Sendai virus vector expressing a soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β and a pharmaceutically acceptable carrier, wherein said vector is infectious and replicates autonomously, but is not disseminative.

14. (Twice Amended) A host cell transfected with a recombinant Sendai virus vector expressing a soluble and biologically active chemokine.

15. (Three Times Amended) A method of inhibiting proliferation of HIV–infected cells *in vitro* which comprises, incubating the host cell of claim 14 *in vitro* under conditions that allow for a secretion of soluble and biologically active chemokine; and contacting said chemokine with cells that are infected with HIV, thereby inhibiting proliferation of HIV-infected cells *in vitro*.

16. (New) The method of claim 7, wherein said CXC-chemokine is soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β.

17. (New) The method of claim 7, wherein the step of recovering comprises the step of removing virions by centrifugation.

18. (New) The method of claim 16, wherein the step of recovering comprises the step of removing virions by centrifugation.

19. (New) The method of claim 10, wherein said CXC-chemokine is soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β.

20. (New) The host of claim 14, wherein said chemokine is soluble and biologically active CXC-chemokine.

21. (New) The host of claim 20, wherein said CXC-chemokine is soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β.

22. (New) A method of inhibiting proliferation of HIV-infected cells *in vitro* which comprises, incubating the host cell of claim 20 *in vitro* under conditions that allow for secretion of soluble and biologically active CXC-chemokine; and contacting said CXC-chemokine with cells that are infected with HIV, thereby inhibiting proliferation of HIV-infected cells *in vitro*.

23. (New) A method of inhibiting proliferation of HIV-infected cells *in vitro* which comprises, incubating the host cell of claim 21 *in vitro* under conditions that allow for secretion of soluble and biologically active stromal cell-derived factor α or stromal cell-derived factor β and contacting said stromal cell-derived factor α or stromal cell-derived β with the cells that are infected with HIV, thereby inhibiting proliferation of HIV-infected cells *in vitro*.